Sequence Compliance

The Examiner has stated that the Sequence Listing previously filed on January 15, 2002 does not include the Sequence shown as Figure 1 and has noted several discrepancies among various peptide sequences presented. Applicants thank the Examiner for bringing this to their attention. A sequence listing for the related case (09/537,858), which the Examiner is also examining, was inadvertently submitted with this case. Applicants provide herewith a corrected Paper Copy of the Sequence Listing and a Computer Readable Form (CRF) thereof. Applicants' agent states that the contents of the corrected Paper Copy of the Sequence Listing and are identical and that the Sequences Listing and CRF do not go beyond the disclosure as originally filed. The specification is amended herewith to indicate sequences listed throughout the specification by the appropriate Sequence Identifiers.

In the Advisory Action mailed August 16, 2002, the Examiner has asserted that it is unclear if the sequence provided for the MCP-2 allelic variant in Figure 1 represents an obvious correction for the sequence provided in the sequence listing. It is unclear what "sequence provided in the sequence listing" is being referred to by the Examiner and Applicants request further clarification from the Examiner so that they may better address the Examiner's question. However, Applicant notes that Figure 1 which was filed in the original application, comprises two sequences, one for anMCP-2 polypeptide according to SEQ ID NO. 2 and one for an allelic variant of the polypeptide (identified in the Sequence listing provided (corresponding to SEQ ID NO. 5). The variant sequence, although left out of the original sequence listing was in the Application as filed. Accordingly, the substitute Sequence Listing provided with the previous Response simply added a sequence identical to that in Figure 1; although this is a correction to the sequence listing, no corrections or alterations of Sequences have been made.

Rejection of Claims 13-16 and 21 Under 35 U.S.C. § 101

Claims 13-16 and 21 stand rejected under 35 U.S.C. § 101 because the Examiner asserts the claims read on non-statutory subject matter, i.e., a product of nature. Applicants submit the rejection is moot in view of the cancellation of the claims. Newly added claims recite isolated truncated forms of MCP-2. Accordingly, Applicants respectfully request that the rejection should be reconsidered and withdrawn.

Rejection of Claims 13-14 and 16-23 Under 35 U.S.C. § 112, Second Paragraph

Claims 13-16 and 18-23 stand rejected under 35 U.S.C. § 112, second paragraph. The Examiner states a number of grounds for these rejections.

Claims 13-14 and 17-23: "lacking...residues 1, 1-2, 1-3, 1-4, or 1-5"

The Examiner asserts that claims 13-14 and 17-23 are indefinite in reciting "lacking...residues 1, 1-2, 1-3, 1-4, or 1-5." The Examiner asserts that it is unclear whether the claims are limited to only deletions of residues, 1, 1-2, 1-3, 1-4 or 1-5, respectively, or whether the claim are directed to proteins which may also comprise additional deletions. Applicants respectfully submit that the rejection is now moot in view of the language of the newly added claims which recite both amino acids lacking and present. Accordingly, Applicants respectfully request that the rejection be reconsidered and withdrawn.

Claims 13-14 and 17-23: "naturally occurring MCP-2"

The Examiner rejects claims over the use of the term "naturally occurring MCP-2 (SEQ ID NO:2)." Although Applicants traverse the rejection, the term "naturally occurring" has been deleted from the newly added claims as being redundant in view of the recitation of SEQ ID NO.

2 and SEQ ID NO: 5). Therefore, Applicants respectfully submit the rejection is now moot and respectfully request that the rejection be reconsidered and withdrawn.

Claim 16: "has the amino acid of SEQ ID NO: 2"

The Examiner states the limitation lacks proper antecedent basis because SEQ ID NO: 5 is not a truncation of SEQ ID NO: 2. Applicants respectfully submit that the rejection is moot in view of the corrected Sequence Listing provided herein and in view of the newly added claims. Accordingly, Applicants respectfully request that the rejection be reconsidered and withdrawn.

Rejection of Claims 13-14, 17 and 23 Under 35 U.S.C. § 102(a)

Claims 13-14, 17 and 23 are rejected as being anticipated by Proost, et al., J. Imunol. 160: 4034-4041, 1998 ("Proost"). The Examiner asserts that Proost teaches an amino-terminally truncated MCP-2 lacking amino acid residues 1-5 of the full length MCP-2). The examiner states, that such a truncated form of MCP-2 would inherently possess the amino acid sequence of SEQ ID NO: 2 which is lacking NH_2-terminal amino acids 1-5. The Examiner further asserts that the truncated MCP-2 is an antagonist of other chemokines, especially MCP-3. Although the Examiner acknowledges that Applicants have an effective priority date to September 29, 1997 for a truncated form of MCP-2 according to SEQ ID 2, lacking residues 1-5 (MCP-2, 6-76), the Examiner states that the priority date of claims 13-14 and 16-23 is considered to be September 28, 1998. Applicants respectfully traverse this grounds of rejection. Proost is cited for the proposition of teaching MCP-2 according to SEQ ID 2, lacking residues 1-5 (MCP-2, 6-76), and discloses this truncated form of MCP-2 after the effective priority date to which the Examiner herself acknowledges Applicants are entitled. Therefore, Proost cannot be prior art for truncated forms of MCP-2, 6-76. To the extent that Proost might be cited as prior art against other types of truncated forms of MCP-2 according to SEQ ID 2 or any truncated forms of its allelic variant

(SEQ ID NO: 5), Proost does not teach these forms and therefore cannot be cited as an anticipating reference under 35 U.S.C. § 102. Accordingly, Applicants respectfully submit that the rejection is improper and should be reconsidered and withdrawn.

Rejection of Claims 13-14 and 17-23 Under 35 U.S.C. § 102(e)

Claims 13-14 and 17-23 are rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 5,739,103 by Rollins, et al. ("Rollins"). The Examiner asserts that Rollins teach amino-terminally truncated chemokines having antagonistic activity and that truncations may be about 1 to about 10 or about 2 to about 7 amino acids. The Examiner further asserts that by teaching recombinant production of the truncated chemokines in eukaryotic cells, this inherently provides a glycosylated protein. Applicants traverse the rejection.

Applicants respectfully submit that the rejection is moot in view of the cancellation of the rejected claims and traverse the rejection to the extent that it might be applied to the newly added claims. Rollins does not teach the specific truncations claimed in Applicants' claims. Further, Rollins does not provide an enabling disclosure of any truncations of an MCP-2 protein which functions as a chemokine antagonist but merely suggests that *any* type of chemokine truncated anywhere in the range described above *might* inhibit binding and *might or might not* function as an inhibitor (see, column 3, line 20, where Rollins acknowledges that the suggested truncated chemokines may or may not inhibit activation of a chemokine receptor responsive to the corresponding endogenous chemokine). However, the only chemokine taught by Rollins is MCP-1. As stated at section 2121.01 of the MPEP, the inquiry in determining whether or not a reference anticipates an invention is to determine whether the reference contains an enabling disclosure. A mere suggestion that a possible range of amino acid truncations in a broad class of different types of chemokines may or may not possess inhibitory activity does not constitute such a disclosure. Accordingly, Applicants respectfully submit that the rejection is improper and

should be reconsidered and withdrawn.

Rejection of Claims 13-23 Under 35 U.S.C. § 103(a)

Claims 13-23 stand rejected under 35 U.S.C. § 103(a) as being obvious in view of Van Damme, et al., J. Exp. Med. 176: 59-65, 1992, (Van Damme) in view of Gong, et al., J. Biol. Chem. 271: 1051-10, 1996 ("Gong") and further in view of Van Coille, et al., Biochem. Biophys. Res. Com. 231: 726-730, 1997 ("Van Coille"). The Examiner asserts that Van Damme teaches purification and characterization of MCP-2 and that Gong teaches MCP-1 truncations and teaches "a broadly applicable method for identifying chemokine antagonists by progressively shortening the amino terminus of MCP-1." The Examiner cites Van Coille for the proposition that there are two alleles of MCP-2. The Examiner asserts that given teachings of Van Damme that "MCP-2 is a structural and functional analog equivalent of MCP-1, the ordinary artisan at the time the invention was made would have been motivated to apply the approach used by Gong, et al....to develop antagonistic amino terminal truncations of MCP-2."

Applicants respectfully traverse the rejection. Gong's statement on page 10523 that residues 1-5 are essential for the "functional activities" of RANTES does not provide a reasonable expectation that truncations of a structurally different chemokine would function as chemokine antagonists, notwithstanding some structural similarities between such chemokines. Gong, in fact, shows variable effects of truncations between the two chemokines RANTES and MCP-1 to chemokine receptors. Additionally, as shown in Figure 6, Gong would lead one of skill in the art away from truncations of *any* kind of chemokine which removed fewer than 5, amino acids, even RANTES, given that truncated RANTES polypeptides taught by Gong with the *fewest* amino acids removed (i.e., RANTES polypeptides consisting of residues 6-68) showed the *least* displacement and therefore the *least* amount of inhibition. Therefore, contrary to the Examiner's assertion, one of skill in the art would *not* be motivated to make truncations with

fewer than six amino acids to obtain an effective chemokine inhibitor given Gong's s teachings that the shortest RANTES polypeptide (e.g., 9-68 amino acids) had the highest affinity for chemokine binding sites (see, page 10525, column 1, lines 13-15) and that longer RANTES polypeptides functioned less effectively as inhibitors. Thus, Gong's teachings would not provide the ordinary artisan with a reasonable expectation that using shorter truncations would provide effective inhibitors. Accordingly, Applicants respectfully submit that the rejection is improper and should be reconsidered and withdrawn.

CONCLUSION

Applicants submit that the claims are allowable and that the Application is now in condition for allowance. Applicants respectfully request early favorable action by the Examiner. If the Examiner believes that a telephone conversation with Applicants' agent would expedite prosecution of this application, the Examiner is cordially invited to call the undersigned agent of record.

Date: Jan 22, 2003

By: _____

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Marked-Up Version of Sections of Specification Showing Changes Being Made

At page 6, please delete line 30,

[Figure 1: shows the amino acid sequence of MCP-2 and of its known variant. Signal]

and insert therefore:

--Figure 1: shows the amino acid sequence of MCP-2 (SEQ ID NO. 1) and of its known variant (SEQ ID NO. 5). Signal--